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# Atherosclerotic Lesions of Supra-Aortic Arteries in Diabetic Patients

Vinko Vidjak<sup>1</sup>, Andrija Hebrang<sup>1</sup>, Boris Brkljačić<sup>2</sup>, Mladen Brajša<sup>1</sup>, Karlo Novačić<sup>1</sup>, Ante Barada<sup>3</sup>, Andrija Škopljanač<sup>4</sup>, Lidija Erdelez<sup>4</sup>, Maja Crnčević<sup>4</sup>, Damir Kučan<sup>4</sup>, Zlata Flegar-Meštrić<sup>5</sup>, Danijela Vrhovski-Hebrang<sup>5</sup> and Goran Roić<sup>6</sup>

<sup>1</sup> Department of Diagnostic and Interventional Radiology, University Hospital »Mercur«, School of Medicine, University of Zagreb, Zagreb, Croatia

<sup>2</sup> Department of Diagnostic and Interventional Radiology, University Hospital »Dubrava«, School of Medicine, University of Zagreb, Zagreb, Croatia

<sup>3</sup> Department of Neurology, University Clinic for Diabetes Endocrinology and Metabolic Diseases »Vuk Vrhovac«, School of Medicine, University of Zagreb, Zagreb, Croatia

<sup>4</sup> Department of Surgery, Division of Vascular Diseases, University Hospital »Mercur«, School of Medicine, University of Zagreb, Zagreb, Croatia

<sup>5</sup> Department of Clinical Chemistry, University Hospital »Mercur«, School of Medicine, University of Zagreb, Zagreb, Croatia

<sup>6</sup> Department of Radiology, Children's University Hospital, School of Medicine, University of Zagreb, Zagreb, Croatia

## ABSTRACT

*The aim of this prospective study was to determine the prevalence and localization of stenotic atherosclerotic lesions of supra-aortic arteries in diabetic patients according to age and sex. Angiograms obtained by digital subtraction angiography were analyzed in 150 diabetic patients (study group) and 150 non-diabetic patients (control group) with symptoms of cerebral ischemia. Diabetic patients were found to have a significantly higher prevalence of stenotic atherosclerotic lesions of the internal carotid artery. Lesions of the large supra-aortic arteries were significantly more common in the left than in the right side of the neck ( $p < 0.001$ ), but the difference between the diabetic and the non-diabetic group did not reach statistical significance. Hemodynamic conditions were found to be more important than diabetes for the occurrence of atherosclerotic lesions in these arteries. Changes in the proximal segment of the left common carotid artery were the most common finding in diabetic patients, hence attention should be paid to this localization on control examinations.*

**Key words:** supra-aortic arteries, diabetes mellitus, atherosclerotic lesions, digital subtraction angiography

## Introduction

Stroke is the third leading cause of death, and atherosclerosis is a major factor in the pathogenesis of ischemic cerebrovascular disease. Almost 31% of lacunar strokes are related to stenosis and thrombosis of great neck arteries<sup>1,2</sup>. On coronary bypass surgery, the risk of stroke is associated with atherosclerotic lesions of supra-aortic arteries in 5 to 19% of cases. It is considerably lower (0–2%) in the absence of atherosclerotic lesions of the aortic arch and of the origin of great supra-aortic arteries. The 6–10.7% risk in patients with coronary artery disease and significant carotid artery stenosis falls to 1.7–2.3% if there is no major carotid artery stenosis<sup>3,4</sup>. It

is therefore of utmost importance to diagnose atherosclerotic changes in supra-aortic arteries.

Atherosclerosis is a diffuse disease with segmental lesions frequently involving particular vessels or their segments. In diabetic patients, these lesions are more extensively, diffusely and unevenly distributed than in non-diabetics, those of lower extremities more frequently involving peripheral arteries (peroneal and tibial arteries)<sup>5–7</sup>. Diabetes mellitus (DM) as a risk factor for atherosclerosis further increases the effect of other risk factors, contributes to the more pronounced macroangiopathic

changes, and increases the incidence of arterial wall calcification<sup>5,6,8</sup>. In diabetic individuals, carotid artery lesions are found even 20 years earlier than in those without diabetes<sup>9</sup>. Determination of the localization and extent of arterial lesions is the basis for optimal choice of therapy<sup>10,11</sup>. With advancements in vascular imaging techniques, the role of non-invasive diagnostic methods (color doppler ultrasonography, computed tomography angiography, magnetic resonance angiography) has gained ever greater importance for their high sensitivity and specificity<sup>12–16</sup>. However, as these noninvasive methods still suffer from some shortcomings, digital subtraction angiography (DSA) remains the gold standard for comparison<sup>17–19</sup>.

The aim of this study was to compare the extent and localization of stenosing lesions of the supra-aortic arteries between diabetic and non-diabetic patients with a history of cerebrovascular disease.

## Patients and Methods

The study included successive patients who had sustained cerebrovascular ischemia, i.e. transient ischemic attack (TIA), reversible ischemic neurologic deficit (RIND) or stroke, between June 1999 and June 2003. Following non-invasive diagnostic tests, 300 patients were referred for DSA by a vascular surgeon or neurologist, because of the still inconclusive findings regarding the degree of the stenotic-obliterating changes of the supra-aortic arteries of the neck, primarily carotid arteries. Patients were divided into two groups of 150 subjects each, according to the presence or absence of DM. Previous laboratory tests were used to rule out non-diabetic population. There was no statistically significant difference between the two patient groups according to clinical lateralization following central ischemia.

In the group of 150 diabetic patients, nine had insulin dependent diabetes mellitus (IDDM) and 141 had non-insulin dependent diabetes mellitus (NIDDM). There were 49 women aged 43–69 (mean age 62) years, and 101 men aged 40–79 (mean age 68) years. Hypertension was present in 97 patients (taking antihypertensive therapy for at least two years), and elevated level of blood lipids in 100 patients (cholesterol >5.2 mmol/L; triglycerides >1.7 mmol/L). Cigarette smoking was reported by 66 patients (>10 cigarettes daily for the last 5 years).

In the group of 150 non-diabetics, there were 52 women aged 46–72 (mean age 64) years, and 98 men aged

44–72 (mean age 69) years. Hypertension was present in 88 patients, cigarette smoking in 90, and hyperlipidemia in 71 patients. Considering risk factors, the proportion of smokers was statistically significantly higher in the group of non-diabetics, and hyperlipidemia in the group of diabetics ( $p < 0.001$  both). The rate of other risk factors showed no statistically significant between-group differences. (Table 1).

DSA was performed using Siemens Angiostar unit (Erlangen, Germany). Informed consent was obtained in writing from each patient prior to the examination. The same technique of supra-aortic artery DSA, consisting of plain transfemoral aortography and selective angiography of each aortic arch branch, was used in all patients. Images of the arteries examined were obtained in two vertical projections and analyzed in approximately real size. Some artery projections were magnified for further grading of stenosis. Each of the arteries analyzed was longitudinally divided into equal thirds (proximal, medial and distal) for more precise stenosis localization. A non-ionic contrast medium, Omnipaque (iohexol, Amersham Health, Oslo, Norway) was injected at a concentration of 350 mg/mL. For selective arteriography a non-ionic contrast medium at a concentration of 300 mg/mL was obligatory. The 5 F catheters for plain and selective angiography were used. Half an hour before the procedure, patients received premedication with intramuscular injection of Apaurin (diazepam, Krka, Novo Mesto, Slovenia) at a concentration of 10 mg/2 mL. Vital functions were monitored during the procedure and an anaesthesiologist was consulted depending on a patient's condition.

Angiographic images of all supra-aortic arteries obtained in diabetic and non-diabetic patients were examined by comparative analysis using double-blind image interpretation. Two independent examiners were blinded for the presence of DM in a particular patient until final result analysis. A coded computer file was created for each individual patient. The analysis included each supra-aortic artery, especially from the origin to its intracranial segment.

The degree of stenosis was determined using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria<sup>20</sup>. Measurements were performed by means of catheters. Results were expressed in appropriate tables of contingency and analyzed by  $\chi^2$ -test. The 0.001 level of significance was used in the interpretation of results.

TABLE 1  
DEMOGRAPHIC DATA AND RISK FACTORS IN DIABETIC AND NON-DIABETIC PATIENTS

| Patients             | Gender  |    | Age (mean years) |    | Hypertension |      | Hyperlipidemia |      | Cigarette smoking |      |
|----------------------|---------|----|------------------|----|--------------|------|----------------|------|-------------------|------|
|                      | M       | F  | M                | F  | n            | %    | n              | %    | n                 | %    |
| Non-diabetic (n=150) | 98      | 52 | 69               | 64 | 88           | 58.6 | 71             | 47.3 | 90                | 60.0 |
| Diabetic (n=150)     | 101     | 49 | 68               | 62 | 97           | 64.6 | 100            | 66.6 | 66                | 44.0 |
|                      | p>0.001 |    | p>0.001          |    | p>0.001      |      | p<0.001        |      | p<0.001           |      |

## Results

Stenosis of the left common carotid artery (CCA) was found in 32.3% of diabetic patients, being three-fold that in non-diabetics (10.0%). Isolated stenoses of the left CCA were found in 32.3%, and multiple stenoses in 1.33% of diabetic patients. Isolated stenoses of the right CCA were also more common in diabetic than in non-diabetic patients (18.0 *vs.* 6.7%). The prevalence of isolated stenoses of both common carotid arteries was statistically significantly higher in the group of diabetic patients ( $p < 0.001$ ) (Table 2).

Isolated stenoses of the left internal carotid artery (ICA) were recorded in 50.7% of diabetic and 29.3% of non-diabetic patients. Multiple stenoses of the left ICA were found in 21.3% of diabetic and 2.0% of non-diabetic patients. Isolated stenoses of the right ICA were detected in 58.0 and 32.7%, and multiple stenoses of the right ICA in 14.0 and 2.0% of diabetic and non-diabetic patients, re-

spectively. The prevalence of isolated and multiple stenoses of both ICA was significantly higher in the group of diabetic patients ( $p < 0.001$ ) (Table 3).

The prevalence of bilateral stenoses of external carotid arteries (ECA) was higher in diabetic patients, but the difference was not statistically significant ( $p > 0.001$ ) (Table 4). Isolated stenoses of the left vertebral artery (VA) were statistically significantly more common ( $p < 0.001$ ) in diabetic (20.0%) than in non-diabetic (5.3%) patients (Table 5), as were stenoses of the right VA and brachiocephalic trunk (BCT) (VA 17.3%; BCT 15.3%) compared to non-diabetic subjects (VA 4.7%; BCT 7.3%). However, the difference was not statistically significant ( $p > 0.001$ ) (Tables 5 and 6). Isolated stenoses of the left subclavian artery (SCA) were statistically significantly more common ( $p < 0.001$ ) in diabetic (26.7%) than in non-diabetic patients (11.3%), whereas the prevalence of the right SCA stenoses showed no between-group difference (6.7% both) (Table 7).

**TABLE 2**  
NUMBER OF COMMON CAROTID ARTERY (CCA) STENOSES

| left CCA    | No stenosis |      | One stenosis |      | Two stenoses |     | Total |     |
|-------------|-------------|------|--------------|------|--------------|-----|-------|-----|
|             | n           | %    | n            | %    | n            | %   | n     | %   |
| Non-DM      | 135         | 90.0 | 15           | 10.0 | 0            | 0.0 | 150   | 100 |
| DM          | 98          | 65.3 | 50           | 32.3 | 2            | 1.3 | 150   | 100 |
| Total       | 233         | 77.7 | 65           | 21.7 | 2            | 0.7 | 300   | 100 |
| $p < 0.001$ |             |      |              | S    |              |     |       |     |

  

| right CCA   | No stenosis |      | One stenosis |      | Two stenoses |     | Total |     |
|-------------|-------------|------|--------------|------|--------------|-----|-------|-----|
|             | n           | %    | n            | %    | n            | %   | n     | %   |
| Non-DM      | 140         | 93.3 | 10           | 6.7  | 0            | 0.0 | 150   | 100 |
| DM          | 122         | 81.3 | 27           | 18.0 | 1            | 0.7 | 150   | 100 |
| Total       | 262         | 87.3 | 37           | 12.3 | 1            | 0.3 | 300   | 100 |
| $p < 0.001$ |             |      |              | S    |              |     |       |     |

CCA – common carotid artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, S – significant

**TABLE 3**  
NUMBER OF INTERNAL CAROTID ARTERY (ICA) STENOSES

| left ICA    | No stenosis |      | One stenosis |      | Two stenoses |      | Three stenoses |     | Total |     |
|-------------|-------------|------|--------------|------|--------------|------|----------------|-----|-------|-----|
|             | n           | %    | n            | %    | n            | %    | n              | %   | n     | %   |
| Non-DM      | 103         | 68.7 | 44           | 29.3 | 3            | 2.0  | 0              | 0.0 | 150   | 100 |
| DM          | 42          | 28.0 | 76           | 50.7 | 31           | 20.7 | 1              | 0.7 | 150   | 100 |
| Total       | 145         | 48.3 | 120          | 40.0 | 34           | 11.3 | 1              | 0.3 | 300   | 100 |
| $p < 0.001$ |             |      |              | S    |              | S    |                |     |       |     |

  

| right ICA   | No stenosis |      | One stenosis |      | Two stenoses |      | Three stenoses |     | Total |     |
|-------------|-------------|------|--------------|------|--------------|------|----------------|-----|-------|-----|
|             | n           | %    | n            | %    | n            | %    | n              | %   | n     | %   |
| Non-DM      | 98          | 65.3 | 49           | 32.7 | 3            | 2.0  | 0              | 0.0 | 150   | 100 |
| DM          | 42          | 28.0 | 87           | 58.0 | 19           | 12.7 | 2              | 1.3 | 150   | 100 |
| Total       | 140         | 46.7 | 136          | 45.3 | 22           | 7.3  | 2              | 0.7 | 300   | 100 |
| $p < 0.001$ |             |      |              | S    |              | S    |                |     |       |     |

ICA – internal carotid artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, S – significant

Analysis of the results indicated the prevalence of lesions of the supra-aortic arteries of the left and right side of the neck to be higher in the left CCA and SCA in comparison with their right counterparts in both diabetic and non-diabetic patients, and statistically significantly higher in the group of diabetic patients ( $p < 0.001$ ).

Stenoses of the proximal segment of the left CCA were detected in 19.3% of diabetic and 7.33% of non-diabetic patients, the difference being statistically significant ( $p < 0.001$ ). The rate of stenoses of the medial and distal segments of the left CCA showed no significant between-group difference ( $p > 0.001$ ). There was no statisti-

**TABLE 4**  
NUMBER OF EXTERNAL CAROTID ARTERY (ECA) STENOSES

| left ECA    | No stenosis |      | One stenosis |      | Total |     |
|-------------|-------------|------|--------------|------|-------|-----|
|             | n           | %    | n            | %    | n     | %   |
| Non-DM      | 132         | 88.0 | 18           | 12.0 | 150   | 100 |
| DM          | 120         | 80.0 | 30           | 20.0 | 150   | 100 |
| Total       | 252         | 84.0 | 48           | 16.0 | 300   | 100 |
| $p < 0.001$ |             |      |              | NS   |       |     |

  

| right ECA   | No stenosis |      | One stenosis |      | Total |     |
|-------------|-------------|------|--------------|------|-------|-----|
|             | n           | %    | n            | %    | n     | %   |
| Non-DM      | 139         | 92.7 | 11           | 7.3  | 150   | 100 |
| DM          | 106         | 70.7 | 44           | 29.3 | 150   | 100 |
| Total       | 245         | 81.7 | 55           | 18.3 | 300   | 100 |
| $p < 0.001$ |             |      |              | NS   |       |     |

ECA – external carotid artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, NS – nonsignificant

**TABLE 5**  
NUMBER OF VERTEBRAL ARTERY (VA) STENOSES

| left VA     | No stenosis |      | One stenosis |      | Total |     |
|-------------|-------------|------|--------------|------|-------|-----|
|             | n           | %    | n            | %    | n     | %   |
| Non-DM      | 142         | 94.7 | 8            | 5.3  | 150   | 100 |
| DM          | 120         | 80.0 | 30           | 20.0 | 150   | 100 |
| Total       | 262         | 87.3 | 38           | 12.7 | 300   | 100 |
| $p < 0.001$ |             |      |              | S    |       |     |

  

| right VA    | No stenosis |      | One stenosis |      | Two stenoses |     | Total |     |
|-------------|-------------|------|--------------|------|--------------|-----|-------|-----|
|             | n           | %    | n            | %    | n            | %   | n     | %   |
| Non-DM      | 143         | 95.3 | 7            | 4.7  | 0            | 0.0 | 150   | 100 |
| DM          | 123         | 82.0 | 26           | 17.3 | 1            | 0.7 | 150   | 100 |
| Total       | 266         | 88.7 | 33           | 11.0 | 1            | 0.3 | 300   | 100 |
| $p < 0.001$ |             |      |              | NS   |              |     |       |     |

VA – vertebral artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, S – significant, NS – non-significant

**TABLE 6**  
NUMBER OF BRACHIOCEPHALIC TRUNK (BCT) STENOSES

| BCT         | No stenosis |      | One stenosis |      | Two stenoses |     | Total |     |
|-------------|-------------|------|--------------|------|--------------|-----|-------|-----|
|             | n           | %    | n            | %    | n            | %   | n     | %   |
| Non-DM      | 137         | 91.3 | 11           | 7.3  | 2            | 1.3 | 150   | 100 |
| DM          | 126         | 84.0 | 23           | 15.3 | 1            | 0.7 | 150   | 100 |
| Total       | 263         | 87.7 | 34           | 11.3 | 3            | 1.0 | 300   | 100 |
| $p < 0.001$ |             |      |              | NS   |              | NS  |       |     |

BCT – brachiocephalic trunk, Non-DM – non-diabetic patient group, DM – diabetic patient group, NS – non-significant

cally significant between-group difference in the rate of stenoses of the right CCA according to localization (Table 8). The rate of stenoses of the left ICA showed no statistically significant between-group difference according to localization either. However, tandem stenoses were more common ( $p < 0.001$ ) in diabetic (21.33%) than in non-diabetic (2.00%) patients (Table 9). There was no statistically significant between-group difference in the rate of the right ICA stenoses according to localization (Table 9).

Stenoses of proximal right ECA were most common in diabetic patients (28.7%) than in non-diabetic patients (7.3%), the difference being statistically significant ( $p < 0.001$ ). Analysis of the results showed no statistical significance in the prevalence of lesions of the left and right ECA (Table 10).

In both diabetic and non-diabetic patients, stenoses of VA were statistically more common ( $p < 0.001$ ) in proximal segments of the artery. Stenoses of the proximal segment of the left VA were detected in 19.3% of diabetic and 4.7% of non-diabetic patients, the difference being statistically significant ( $p < 0.001$ ). There was no statistically significant between-group difference in the prevalence of stenoses of the medial segment of the left VA. Stenoses of the proximal segment of the right VA were found in 16.7% of diabetic and 4.7% of non-diabetic patients, the difference being statistically significant ( $p < 0.001$ ). There was no statistically significant between-group difference in the rate of VA stenoses at other localizations (Table 11).

**TABLE 7**  
NUMBER OF SUBCLAVIAN ARTERY (SCA) STENOSES

| left SCA    | No stenosis |      | One stenosis |      | Two stenoses |     | Total |     |   |   |
|-------------|-------------|------|--------------|------|--------------|-----|-------|-----|---|---|
|             | n           | %    | n            | %    | n            | %   | n     | %   | n | % |
| Non-DM      | 132         | 88.0 | 17           | 11.3 | 1            | 0.7 | 150   | 100 |   |   |
| DM          | 108         | 72.0 | 40           | 26.7 | 2            | 1.3 | 150   | 100 |   |   |
| Total       | 240         | 80.0 | 57           | 19.0 | 3            | 1.0 | 300   | 100 |   |   |
| $p < 0.001$ |             |      |              | S    |              | NS  |       |     |   |   |

  

| right SCA   | No stenosis |      | One stenosis |     | Two stenoses |     | Three Stenoses |     | Total |     |
|-------------|-------------|------|--------------|-----|--------------|-----|----------------|-----|-------|-----|
|             | n           | %    | n            | %   | n            | %   | n              | %   | n     | %   |
| Non-DM      | 139         | 92.7 | 10           | 6.7 | 0            | 0.0 | 1              | 0.7 | 150   | 100 |
| DM          | 139         | 92.7 | 10           | 6.7 | 1            | 0.7 | 0              | 0.0 | 150   | 100 |
| Total       | 278         | 92.7 | 20           | 6.7 | 1            | 0.3 | 1              | 0.3 | 300   | 100 |
| $p < 0.001$ |             |      |              | NS  |              |     |                |     |       |     |

SCA – subclavian artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, S – significant, NS – non-significant

**TABLE 8**  
COMMON CAROTID ARTERY (CCA) STENOSES ACCORDING TO LOCALIZATION

| left CCA    | No stenosis |      | Proximal segment |      | Medial segment |     | Distal segment |     | Tandem |     | Total |     |
|-------------|-------------|------|------------------|------|----------------|-----|----------------|-----|--------|-----|-------|-----|
|             | n           | %    | n                | %    | n              | %   | n              | %   | n      | %   | n     | %   |
| Non-DM      | 135         | 90.0 | 11               | 7.3  | 1              | 0.7 | 3              | 2.0 | 0      | 0.0 | 150   | 100 |
| DM          | 98          | 65.3 | 29               | 19.3 | 11             | 7.3 | 10             | 6.7 | 2      | 1.3 | 150   | 100 |
| Total       | 233         | 77.7 | 40               | 13.3 | 12             | 4.0 | 13             | 4.3 | 2      | 0.7 | 300   | 100 |
| $p < 0.001$ |             |      |                  | S    |                | NS  |                | NS  |        |     |       |     |

  

| right CCA   | No stenosis |      | Proximal segment |     | Medial segment |     | Distal Segment |     | Tandem |     | Total |     |
|-------------|-------------|------|------------------|-----|----------------|-----|----------------|-----|--------|-----|-------|-----|
|             | n           | %    | n                | %   | n              | %   | n              | %   | n      | %   | n     | %   |
| Non-DM      | 140         | 93.3 | 4                | 2.7 | 1              | 0.7 | 5              | 3.3 | 0      | 0.0 | 150   | 100 |
| DM          | 122         | 81.3 | 10               | 6.7 | 4              | 2.7 | 13             | 8.7 | 1      | 0.7 | 150   | 100 |
| Total       | 262         | 87.3 | 14               | 4.7 | 5              | 1.7 | 18             | 6.0 | 1      | 0.3 | 300   | 100 |
| $p < 0.001$ |             |      |                  | NS  |                | NS  |                | NS  |        |     |       |     |

CCA – common carotid artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, S – significant, NS – non-significant

**TABLE 9**  
INTERNAL CAROTID ARTERY (ICA) STENOSES ACCORDING TO LOCALIZATION

| left ICA | No stenosis |      | Proximal segment |      | Medial segment |     | Distal segment |     | Tandem |      | Total |     |
|----------|-------------|------|------------------|------|----------------|-----|----------------|-----|--------|------|-------|-----|
|          | n           | %    | n                | %    | n              | %   | n              | %   | n      | %    | n     | %   |
| Non-DM   | 103         | 68.7 | 41               | 27.3 | 0              | 0.0 | 3              | 2.0 | 3      | 2.0  | 150   | 100 |
| DM       | 42          | 28.0 | 62               | 41.3 | 5              | 3.3 | 9              | 6.0 | 32     | 21.3 | 150   | 100 |
| Total    | 145         | 48.3 | 103              | 34.3 | 5              | 1.7 | 12             | 4.0 | 35     | 11.3 | 150   | 100 |
| p<0.001  |             |      | NS               |      |                |     | NS             |     | S      |      |       |     |

  

| right ICA | No stenosis |      | Proximal segment |      | Medial segment |     | Distal segment |     | Tandem |      | Total |     |
|-----------|-------------|------|------------------|------|----------------|-----|----------------|-----|--------|------|-------|-----|
|           | n           | %    | n                | %    | n              | %   | n              | %   | n      | %    | n     | %   |
| Non-DM    | 98          | 65.3 | 48               | 32.0 | 0              | 0.0 | 1              | 0.7 | 3      | 2.0  | 150   | 100 |
| DM        | 42          | 28.0 | 74               | 49.3 | 3              | 2.0 | 10             | 6.7 | 21     | 14.0 | 150   | 100 |
| Total     | 140         | 46.7 | 122              | 40.7 | 3              | 1.0 | 11             | 3.7 | 24     | 16.0 | 150   | 100 |
| p<0.001   |             |      | NS               |      |                |     | NS             |     | NS     |      |       |     |

ICA – internal carotid artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, S – significant, NS – non-significant

**TABLE 10**  
EXTERNAL CAROTID ARTERY (ECA) STENOSES ACCORDING TO LOCALIZATION

| left ECA | No stenosis |      | Proximal segment |      | Total |     |
|----------|-------------|------|------------------|------|-------|-----|
|          | n           | %    | n                | %    | n     | %   |
| Non-DM   | 132         | 88.0 | 18               | 12.0 | 150   | 100 |
| DM       | 120         | 80.0 | 30               | 20.0 | 150   | 100 |
| Total    | 252         | 84.0 | 48               | 16.0 | 300   | 100 |
| p<0.001  |             |      | NS               |      |       |     |

  

| right ECA | No stenosis |      | Proximal segment |      | Medial segment |     | Total |     |
|-----------|-------------|------|------------------|------|----------------|-----|-------|-----|
|           | n           | %    | n                | %    | n              | %   | n     | %   |
| Non-DM    | 139         | 92.7 | 11               | 7.3  | 0              | 0.0 | 150   | 100 |
| DM        | 106         | 70.7 | 43               | 28.7 | 1              | 0.7 | 150   | 100 |
| Total     | 245         | 81.7 | 54               | 18.0 | 1              | 0.3 | 300   | 100 |
| p<0.001   |             |      | S                |      |                |     |       |     |

ECA – external carotid artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, S – significant, NS – non-significant

Stenoses of proximal BCT were the most common of all localizations in both patient groups; however, the difference in the rate of stenoses according to localization did not reach statistical significance (Table 12).

Proximal segments of both SCA were the most common localization of arterial stenoses. No statistically significant between-group difference was found in the prevalence of these stenoses (Table 13).

Atherosclerotic stenoses of the supra-aortic arteries of the neck were most frequently observed in the 60–69 age group of both diabetic and non-diabetic patients. There was no significant between-group difference in the prevalence of these lesions according to age.

## Discussion

The prevalence, localization and morphological features of atherosclerotic plaques have been thoroughly in-

vestigated in peripheral artery angiograms of diabetic patients involved<sup>8,21,22</sup>. Results of the present study appear to be quite intriguing in terms of morphological characteristics of supra-aortic artery atherosclerosis in diabetic patients. The hypothesis that the morphological features of atherosclerotic lesions of supra-aortic arteries are similar to those found on peripheral arteries of diabetic individuals was not confirmed. Some properties of atherosclerotic lesions of supra-aortic arteries in diabetic patients, such as localization of stenoses and occurrence of arterial atherosclerosis at a younger age, yielded rather unexpected results in the supra-aortic arteries of our diabetic subjects. The prevalence of atherosclerotic stenoses according to the duration of DM varied among particular arteries. Comparison between diabetic and non-diabetic patients revealed a statistically significantly greater number of stenoses of both common and both internal carotid arteries in the former; an important, yet

expected finding. The causes of cerebrovascular ischemia are most frequently associated with lesions of these arteries, thus explaining the higher prevalence of cerebral ischemia in diabetic *versus* non-diabetic patients<sup>9,23–26</sup>.

Analysis of multiple stenoses of the same artery also yielded results as expected. These lesions were significantly more frequently recorded in diabetic patients, but only in internal carotid arteries, whereas between-group

**TABLE 11**  
VERTEBRAL ARTERY (VA) STENOSES ACCORDING TO LOCALIZATION

| left VA | No Stenosis |      | Proximal segment |      | Medial segment |     | Total |     |
|---------|-------------|------|------------------|------|----------------|-----|-------|-----|
|         | n           | %    | n                | %    | n              | %   | n     | %   |
| Non-DM  | 142         | 94.7 | 7                | 4.7  | 1              | 0.7 | 150   | 100 |
| DM      | 120         | 80.0 | 29               | 19.3 | 1              | 0.7 | 150   | 100 |
| Total   | 262         | 87.3 | 36               | 12.0 | 2              | 0.7 | 300   | 100 |
| p<0.001 |             |      |                  | S    |                | NS  |       |     |

  

| right VA | No stenosis |      | Proximal segment |      | Medial segment |     | Tandem |     | Total |     |
|----------|-------------|------|------------------|------|----------------|-----|--------|-----|-------|-----|
|          | n           | %    | n                | %    | n              | %   | n      | %   | n     | %   |
| Non-DM   | 143         | 95.3 | 7                | 4.7  | 0              | 0.0 | 0      | 0.0 | 150   | 100 |
| DM       | 123         | 82.0 | 25               | 16.7 | 1              | 0.7 | 1      | 0.7 | 150   | 100 |
| Total    | 266         | 82.3 | 32               | 10.7 | 1              | 0.3 | 1      | 0.3 | 300   | 100 |
| p<0.001  |             |      |                  | S    |                |     |        |     |       |     |

VA – vertebral artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, S – significant, NS – non-significant

**TABLE 12**  
BRACHIOCEPHALIC TRUNK (BCT) STENOSES ACCORDING TO LOCALIZATION

| BCT     | No stenosis |      | Proximal segment |      | Medial segment |     | Tandem |     | Total |     |
|---------|-------------|------|------------------|------|----------------|-----|--------|-----|-------|-----|
|         | n           | %    | n                | %    | n              | %   | n      | %   | n     | %   |
| Non-DM  | 137         | 91.3 | 8                | 5.3  | 3              | 2.0 | 2      | 1.3 | 150   | 100 |
| DM      | 126         | 84.0 | 20               | 13.3 | 3              | 2.0 | 1      | 0.7 | 150   | 100 |
| Total   | 263         | 87.7 | 28               | 9.3  | 6              | 2.0 | 3      | 1.0 | 300   | 100 |
| p<0.001 |             |      |                  | NS   |                | NS  |        | NS  |       |     |

BCT – brachiocephalic trunk, Non-DM – non-diabetic patient group, DM – diabetic patient group, NS – non-significant

**TABLE 13**  
SUBCLAVIAN ARTERY (SCA) STENOSES ACCORDING TO LOCALIZATION

| left SCA | No stenosis |      | Proximal segment |      | Medial segment |      | Distal segment |     | Tandem |     | Total |     |
|----------|-------------|------|------------------|------|----------------|------|----------------|-----|--------|-----|-------|-----|
|          | n           | %    | n                | %    | n              | %    | n              | %   | n      | %   | n     | %   |
| Non-DM   | 132         | 88.0 | 10               | 6.7  | 7              | 4.7  | 0              | 0.0 | 1      | 0.7 | 150   | 100 |
| DM       | 108         | 72.0 | 18               | 12.0 | 17             | 11.3 | 5              | 3.3 | 2      | 1.3 | 150   | 100 |
| Total    | 240         | 80.0 | 28               | 9.3  | 24             | 8.0  | 5              | 1.7 | 3      | 1.0 | 300   | 100 |
| p<0.001  |             |      |                  | NS   |                | NS   |                |     |        | NS  |       |     |

  

| right SCA | No stenosis |      | Proximal segment |     | Medial segment |     | Tandem |     | Total |     |
|-----------|-------------|------|------------------|-----|----------------|-----|--------|-----|-------|-----|
|           | n           | %    | n                | %   | n              | %   | n      | %   | n     | %   |
| Non-DM    | 139         | 92.7 | 8                | 5.3 | 2              | 1.3 | 1      | 0.7 | 150   | 100 |
| DM        | 139         | 92.7 | 8                | 5.3 | 2              | 1.3 | 1      | 0.7 | 150   | 100 |
| Total     | 278         | 92.7 | 16               | 5.3 | 4              | 1.3 | 2      | 0.7 | 300   | 100 |
| p<0.001   |             |      |                  | NS  |                | NS  |        | NS  |       |     |

SCA – subclavian artery, Non-DM – non-diabetic patient group, DM – diabetic patient group, NS – non-significant



differences for all other arteries were not statistically significant. These findings need not have a substantial impact on the clinical picture or expected course of cerebral ischemia, as the number of stenoses in internal carotid arteries usually has no major clinical relevance. However, the presence of multiple stenoses may hamper interventional radiological procedures or surgical treatment of internal carotid artery<sup>27</sup>. It should therefore be borne in mind that the presence of multiple stenoses is more likely in diabetic individuals.

Results on other arteries showed that there was no statistically significant difference between the diabetic and the non-diabetic group of patients in the number of stenoses of external carotid arteries on either side. This might be due to the substantially different role of internal and external carotid arteries, the former being conductive and the latter terminal by function. These findings greatly differed from those recorded on peripheral arteries, where atherosclerotic lesions on terminal arteries were more pronounced and those on conductive arteries less pronounced in diabetic patients as compared to non-diabetic individuals<sup>8,22</sup>.

Other conductive supra-aortic arteries showed a rather regular pattern in the number of stenoses in diabetics as compared with non-diabetics. Interestingly enough, there were no statistically significant between-group differences in the number of stenoses on the right side of the aortic arch, i.e. on the right subclavian artery and vertebral artery. In contrast, stenoses of the left subclavian artery and vertebral artery were considerably more common in diabetic patients. This difference could be ascribed to hemodynamic properties of the respective arteries rather than to the presence of DM. On the right side of the aortic arch, the arteries do not originate directly from the arch, but from the brachiocephalic trunk, which therefore sustains most of the lesions induced by change in the flow direction upon blood shunt from the aorta to the arch branches. Our finding of the significantly greater prevalence of brachiocephalic trunk lesions in diabetic patients is consistent with this hypothesis. In contrast to arteries on the right side of the neck, the left subclavian artery originates directly from the aorta, thus being at a higher exposure to hemodynamic changes than its contralateral counterpart. This would also explain the left-to-right difference in the number of atherosclerotic lesions.

The possible effect of hemodynamics on the results obtained is best illustrated by the findings recorded for subclavian arteries. The considerably greater number of stenoses detected on the left side in both groups of patients pointed to a conclusion that diabetes was not the cause of these lesions. In the group of non-diabetic patients, 17 stenoses were recorded in the left subclavian artery, whereas only 7 were recorded in the right one. The difference was even greater in the group of diabetic patients, where 40 stenoses were found in the left subclavian artery and only 10 in its right counterpart. In total, the left subclavian artery was narrowed in 57, and right subclavian artery in only 20 patients. These obser-

vations may play a major role in daily routine, e.g., on measuring blood pressure, planning a percutaneous approach from the upper extremity, etc.

Stenoses of the common carotid artery belong to the lesions that can be successfully treated by percutaneous angioplasty and stenting or operation, which makes this localization of pathologic changes highly important. In our study, diabetic patients had a significantly greater prevalence of stenoses of the left common carotid artery than non-diabetic patients. No such between-group difference was observed for the right common carotid artery. The total number of stenoses in both diabetic and non-diabetic patients was greater in the left common carotid artery ( $n=67$ ) than in its right counterpart ( $n=38$ ). Comparison of the two groups in separate revealed an interesting pattern. Diabetic patients had 28 stenoses on the right side and 52 stenoses, i.e. almost twofold, on the left side. Patients without diabetes had 10 stenoses on the right side and 15 stenoses on the left side. These figures indicate that hemodynamic variation between the left and the right common carotid arteries influenced the prevalence of atherosclerotic lesions in both patient groups, the difference between the two sides being greater in diabetic patients. Thus, a higher rate of pathologic changes in the left common carotid artery can be expected in diabetic individuals, warranting caution on control examination of carotid arteries in these patients. In contrast, it is of great importance to detect lesions of internal carotid artery because they are treatable, yet showing no difference between the left and the right side in either diabetic or non-diabetic patients.

Overall, diabetic patients had a higher rate of changes in the common carotid artery than non-diabetics. The present study also revealed that stenoses affected proximal segments of the left common carotid artery significantly more frequently in diabetic patients, whereas in non-diabetics there was no significant difference according to localization of the lesions, although they were also more frequently recorded on the left side. These findings suggest that proximal stenoses of the left common carotid artery should be specifically looked for in diabetic patients, where these lesions are considerably more common than in non-diabetics. These changes may pose a diagnostic problem, proximal stenoses being difficult to visualize and analyze by doppler technique. Therefore, other methods should be employed to search for possible proximal lesions of the common carotid artery in diabetic patients, including angiography, non-invasive computer tomography angiography, and magnetic resonance angiography. Our results pointed to inadequacy of doppler examination of the carotid arteries in diabetic patients. Of course, the use of a particular method of artery visualization depends primarily on the clinical picture, and the results of this study should be considered as potentially useful guidelines to diabetologists.

Study of the relationship between proximal and distal lesions has a diagnostic value in pointing to the expected localization of a possible stenosis. The only statistically significantly more prevalent proximal localization was

observed on the left common carotid artery, whereas on the right common carotid artery stenoses were located in the proximal and distal segments at an equal rate. This could be explained by the above mentioned hemodynamic differences due to the left artery originating directly from the aortic arch. Of other arteries, only both vertebral arteries showed a higher prevalence of proximal localization of pathologic changes at the very origin of subclavian arteries. This finding is relevant for the diagnosis of ischemia of the posterior cranial fossa, pointing to the site that should definitely be visualized on diagnostic work-up<sup>28,29</sup>.

The analysis of the results of the effect of age and sex on supra-aortic artery atherosclerosis in diabetic patients and the control group of non-diabetic patients suggested a similar conclusion. Literature data suggest that men are prone to atherosclerotic changes of peripheral arteries up to 75 years of age<sup>30</sup>. Age difference was not found to have any major impact on the prevalence of stenotic-obliterating changes in supra-aortic arteries in either diabetic or non-diabetic patients. In both patient groups, the maximal prevalence of these lesions was recorded in the 60–69 age group. There is no doubt that diabetes contributes additionally to the progression of

atherosclerotic lesions of supra-aortic arteries, as indicated by their higher prevalence in the group of diabetic patients. Nevertheless, no correlation was found with the earlier occurrence of cerebral ischemia in diabetic patients.

Correlation of the lesions with sex produced no significant difference between diabetic and non-diabetic patients for any of the supra-aortic arteries examined. Diabetes did not cause either uniform development of stenoses on any of the supra-aortic arteries examined or their higher prevalence according to sex. Diabetes as a risk factor did not increase the prevalence of supra-aortic artery lesions in either sex, as has been reported for peripheral arteries in men or coronary arteries in women.

These findings may prove clinically useful in the follow-up of diabetic patients, the choice of diagnostic procedures as well as in active treatment either by atereectomy or by percutaneous angioplasty and stenting.

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V. Vidjak

Department of Diagnostic and Interventional Radiology, University Hospital »Mercur«, Zajčeva 19, HR-10000 Zagreb, Croatia

e-mail: vinko.vidjak@zg.t-com.hr

## **ATEROSKLEROTSKE PROMJENE SUPRAAORTNIH ARTERIJA U BOLESNIKA SA ŠEĆERNOM BOLEŠĆU**

### **S A Ž E T A K**

Cilj ovog prospektivnog istraživanja bio je odrediti prevalenciju i lokalizaciju stenotičnih aterosklerotskih lezija supraaortnih arterija u bolesnika sa šećernom bolešću prema dobi i spolu. Analizirani su angiogrami dobiveni digitalnom suptrakcijskom angiografijom u 150 bolesnika sa šećernom bolešću (ispitivana skupina) i 150 bolesnika bez šećerne bolesti (kontrolna skupina) sa simptomima cerebralne ishemije. Ustanovljeno je da bolesnici sa šećernom bolešću imaju značajno višu prevalenciju stenotičnih aterosklerotskih lezija unutarne karotidne arterije. Lezije velikih supraaortnih arterija bile su češće na lijevoj nego na desnoj strani vrata ( $p < 0,001$ ), međutim razlika između dijabetičke i nedijabetičke skupine nije bila statistički značajna. Hemodinamika je imala značajniju ulogu od šećerne bolesti u stvaranju aterosklerotskih lezija ovih arterija. Budući da su kod bolesnika sa šećernom bolešću najčešći nalaz bile promjene proksimalnog segmenta lijeve zajedničke karotidne arterije, pri kontrolnim pregledima trebalo bi posvetiti pozornost toj lokalizaciji.